REMARKS/ARGUMENTS

Applicants submit this response to the Official Action dated September 29, 2003. Applicants thank the Examiner for review of the identified Application, and for the courtesy of a telephone interview on March 9, 2004, during which the various rejections were discussed. In particular, the interview established that demonstrating entitlement to a genus claim for the nucleic acid under 35 U.S.C. § 102 with respect to wild-type as well as mutant variants would also address the issues under 35 U.S.C. § 112. Applicants now request reconsideration in light of the amended claims and supporting remarks/arguments. Applicants have sought appropriate records to support a Declaration under 37 C.F.R. § 1.131. Accordingly, the delay in filing this response is not undue.

Status of Claims

Claims 1-2 and 5 have been amended.

Claims 12, 16, 20, 23, and 33 (even though withdrawn) have also been amended.

Claim 39 is new.

No new matter has been added.

Claims 8-11, 28-32, and 36-38 have been cancelled without prejudice as drawn to a non-elected invention. Applicants reserve the right to prosecute the subject matter of these claims in a related continuing application.

Claims 1-7, 12-27, 33-35, and 39 are presently pending.

Claims 1-7 and 33-35 stand rejected.

Election/Restriction

The examiner has made the Restriction Requirement final, stating that neither the diagnostic process of Group IV (claims 12-22) nor the kit of Group V (23-28) produces or uses

the nucleic acid of the claims of Group 1. In response, Applicants have amended the claims so that claims 12-27 now require the use of the elected nucleic acids. In addition, Applicants have cancelled claim 28 as it requires the use of the unelected antibody from claim 11. Because of these amendments, Applicants now request a rejoinder of the amended claims in this section.

Rejection under 35 U.S.C. § 101

The examiner has rejected Claims 1-7 as directed to non-statutory matter, the claims referring to nucleic acid sequences found in human subjects. In response, Applicants have amended these claims by reciting an "isolated" nucleic acid, consistent with our disclosure in the specification, and as helpfully suggested by the Examiner. Since these claims are now drawn to statutory matter, grounds for rejection under this provision are no longer applicable.

Rejection under 35 U.S.C. § 112: Written Description

The examiner has rejected Claims 1-2 and 4-6 as failing to comply with the written description requirement. In response, Applicants request that the Examiner consider the following actions and remarks:

(1) Applicants have removed from Claim 1 the limiting phrase "encoding a MCOLN1 polypeptide, wherein a mutation of a MCOLN1 gene encoding the MCOLN1 polypeptide results in a defect in expression of a functional MCOLN1." As a result, claim 1 has written support in the specification, which describes the MCOLN1 gene as encompassing SEQ ID NO:1 and SEQ ID NO:2.

(2) Notwithstanding the above, the Examiner confirms that "the instant application provides a detailed description of a number of isolated DNAs encoding particular *MCOLN1* genes having very specific physical and structural properties," but also contends that "the instant specification does not provide a structural formula which is definitive of all human *MCOLN1* genes having a mutation that 'results in a defect in expression of a functional *MCOLN1*." To support this position, the Examiner relies on the Federal Circuit's decision in *The Regents of the University of California v. Eli Lilly and Company,* 119 F.3d 1559 (CAFC 1997) (hereinafter *Lilly*). In response, Applicants wish to raise three independent arguments why the generic claims to mutations in MCOLN1 have written support in the description, fully consistent with the *Lilly* decision.

First, whereas the *Lilly* patent fails to disclose any nucleic acid sequence for human insulin cDNA, the instant application discloses extensive nucleic acid sequence for generic MCOLN1 mutations: they are disruptions of disclosed nucleic acid sequences (SEQ ID NO:1 and NO:2) that by their very nature (insertion, deletion, missense, nonsense, frameshift, splice site etc.) necessarily disrupt function of the encoded protein identified in SEQ ID NO: 3. This description reveals *what* MCON1 mutations are--not a plan for obtaining them. Accordingly, this description readily conforms with *Lilly's* holding that: "[a]n adequate description of a DNA, such as the cDNA of the recombinant plasmids . . . 'requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for claiming the claimed chemical invention." *Id.* at 1556 (the court quoting *Fiers v. Revel, 984 F.2d 1164, 1171*).

Second, Applicants point to the detailed language in the specification, describing the extensive biochemical and clinical abormalities triggered by MCOLN1 mutations. These include, for example, corneal clouding; abnormal presence of storage bodies and large vacuoles in many cell

types; lysosomal inclusions (despite normal levels of lysosomal hydrolases); defects in secretion, nerve conductance, and cell signaling; and growth and pyschomotor retardation. Such exensive phenotypic description, a hallmark of clinical genetics, allows one of ordinary skill in the art to readily distinguish mutations in MCOLN1 from silent polymorphic changes. Accordingly, the disclosed phenotypic description of MCOLN1 mutants is fully consistent with the court's holding in *Lilly* that "it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language.'" *Id.* at 1560.

Third, Applicants wish to argue that the Examiner has not properly considered the level of ordinary skill in the art of genetics. As the *Lilly* court stated: "[t]o fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that 'the inventor claimed the claimed invention'". *Id at.* 1566 (the court quoting *Lockwood v. American Airlines, 107 F.3d 1565, 172).* With respect to species/genus claims, such as generic claims to MCOLN1 mutations, MPEP § 2163 states that:

> What constitutes a representative number {of species} is an *inverse function* (emphasis added) of the skill and knowledge in the art. Satisfactory disclosure of a 'representative number' depends on whether of one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed.

With respect to the instant application -- filed twenty-four years after the *Lilly* application -- one with ordinary skill in the art of molecular genetics will recognize that the Applicants are in possession of the genus of mutations in claim 2. The specification presents an extensive list of isolated mutations, all of which: (i) map to the MCOLN1 locus; (ii) disrupt proper expression of the MCOLN1 product; and (iii) correlate with the unique etiological profile of mucolipidosis.

For these reasons, Applicants respectfully submit that the grounds for rejecting the claims under this provision are inapplicable.

Rejection under 35 U.S.C. § 112: Second Paragraph

The examiner has rejected Claims 1-7 and 33-35 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In response, the Applicants request that the Examiner consider the following three actions and remarks:

(1) As noted above, Applicants have amended Claim 1, including removal of the term "mutation", which obviates the examiner's concern for lack of clarity.

(2) The Examiner has contended that the term "MCOLN1" is indefinite. Since all the claims relate to structure (SEQ ID NO: 3) as well as function (characteristics of MCOLN1), there is no ambiguity to the skilled artesian. Furthermore, claim 1 as amended no longer recites this term.

(3) Applicants have also removed the term "about" from independent claims 1 and 33, thus addressing this basis for rejection. Since any measurement has a certain intrinsic error, removing the term "about" from the claim does not affect claim scope.

On the basis of these changes and remarks, Applicants respectfully submit that the grounds for rejecting these claims under this provision are inapplicable.

Rejection under 35 U.S.C. § 102(e)

The examiner has rejected claims 1, 5-7 and 33-35 as being anticipated by the Curtis et al. and Lal et al. patent publications, with effective filing dates of April 7, 2000 and August 17, 1999, respectively. According to the examiner, these publications anticipate clams to nucleic acids encoding MCOLN1, corresponding amino acid sequence, and expression vectors comprising the nucleic acid.

In response, Applicants have provided a Declaration under 37 C.F.R. § 1.131. The declaration establishes reduction to practice of the subject matter of claims 1, 5-7, and 33-34, prior to August 17, 1999. With respect to claim 35, Applicants note that the Curtis et al. and Lal et al. publications do not claim mutations in the disclosed gene, nor do they disclose specific functional or genetic links between the gene and disease, including mucolipidosis conditions, such as MLIV. Since neither reference identifies a disease or disorder that associates with a defect in MCOLN1 expression, there is no express teaching, or even any suggestion, in either reference to prepare a phramaceutical composition comprising an expression vector for MCOLN1. Accordingly, including this claim in an anticipation rejection was an error. Moreover, with no suggestion, much less an express teaching of a disease or condition that might be treated with MCOLN1, neither reference renders the invention obvious, whether taken alone or in combination.

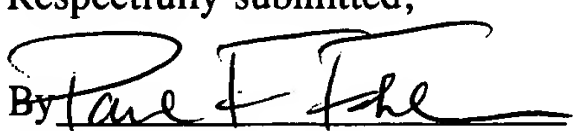
In light of the accompanying Rule 1.131 Declaration and the foregoing argument, the Examiner's rejection is overcome in part, and in error in part. Applicants respectfully request withdrawal of this rejection.

CONCLUSION

In view of the above, Applicants believe that each of the presently pending claims in this application is in immediate condition for allowance. Accordingly, Applicants respectfully request Examiner to pass this application to issue.

Dated: June 21, 2004

Respectfully submitted,

By 

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